REMARKS

Claims 1-40 were pending in the application. Claims 1-9, 11-21, 23-36, and 38-40 were under active consideration following withdrawal of Claims 10, 22, and 37 as non-elected species. Claims 12, 13, 16, 21, 23, 27, 28, 30, and 39 have been amended. Upon entry of these amendments, Claims 1-40 will be pending with Claims 1-9, 11-21, 23-36, and 38-40 under active consideration. Claims 1, 16, and 21-23 are independent.

Applicants submit respectfully that the amendments presented herein are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

The specification is amended to insert the appropriate Sequence Identifiers at page 40, lines 20-28, accordance with 37 C.F.R Section 1.821(d) and as required by the Examiner. Applicants note that a separate sequence listing was provided June 5, 2003, as Paper No. 17.

The references listed on the IDS of February 8, 2002, will be submitted under separate cover. The Examiner is requested to consider all of the references in due course prior to allowance of the present application.

Claim 13 is amended to change its dependency to Claim 12.

Claims 12, 23, 27, 28, 30, and 39 are amended to remove the term "substantially."

Claims 16, 21, and 23 have been amended to point out more particularly and claim more distinctly that which Applicants regard as their invention by now reciting that the obtained tissues are not suitable for transplantation. The amendments find support throughout the specification and claims as filed, particularly in Claim 1 as filed.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. The Rejections Under 35 U.S.C. §§ 102(b) And (e) Should Be Withdrawn

A. The Rejection Over Reid

The Office Action, at pages 4-5, rejects Claims 1-9, 11-12, 16-17, 19-20, and 39-40 as allegedly being anticipated by Published PCT Application No. WO 95/13697 to Reid *et al.* (hereinafter, "Reid"), under 35 U.S.C. § 102(b) for the reasons of record. In sum, the Office Action alleges that Reid discloses methods of isolating hepatic precursors from donors no longer having a heartbeat. Applicants traverse respectfully.

Applicants submit respectfully that the rejected claims, as amended, are not anticipated by Reid because Reid does not disclose each and every element of those amended claims as is required for a *prima facie* showing of anticipation. In particular, Claims 1 and 16, 21, and 23, as amended, are directed to a method of processing non-fetal donor tissue to obtain an enriched population of progenitor cells comprising providing non-fetal donor tissue that would be considered unsuitable for an organ

transplantation. Applicants submit respectfully that Reid does not teach or suggest a method of obtaining progenitor cells from tissue that would be unsuitable for transplantation.

The present specification, as filed, teaches that tissue is considered unsuitable for organ transplantation after the tissue has been exposed to a period of ischemia; in particular, warm ischemia (see, for example, page 21, lines 30-31, and page 3, lines 15-18, of the specification as filed). One skilled in the art is able to determine a time, after cessation of the donor's heartbeat, when an organ is no longer useful for transplantion; *i.e.*, when the organ has suffered irreversible damage and has become "useless" (see page 4, lines 2-12, of the specification as filed). The specification also teaches that organ tissue may be preserved for transplantation by use of preservative techniques (see page 3, line 30, to page 4, line 2. It is well known in the art that chilling and storing an organ on ice immediately following harvesting the organ from the donor is one prominent means of preserving organ tissue for transplantation.

The Office Action rejects the subject claims on the basis that the method of harvesting organ tissue disclosed in Reid teaches the isolation of hepatic progenitor cells from a non-beating heart donor (because the process of dissecting out the organ results in the death of the donor), and that such isolation is allegedly the subject matter of the present claims (*e.g.*, Claims 2-5). Respectfully, Applicants disagree. While the present claims, as variously amended, recite that the donor is a non-beating heart donor, the claims also require that the donor organ tissue be unsuitable for transplantation (See, for example, Claim 1). The method disclosed by Reid at page 14,

lines 9-15, as noted in the Office Action, provides that the organ tissue is harvested on ice and thereafter stored immediately on ice prior to isolation of the progenitor cells. Accordingly, Applicants submit respectfully that the organ tissue used in the method of Reid was **not** unsuitable for transplant. Therefore, despite the Office Action's allegation that the liver tissues were harvested within the recited time windows, the disclosed method did not teach each and every element of the claimed method; *i.e.*, the disclosed method did not teach that the tissue was unsuitable for transplantation.

In view of the above, Applicants submit respectfully that the claims of the present invention, as amended, are not anticipated by Reid. Accordingly, Applicants request respectfully that the rejection to Claims 1-9, 11-12, 16-17, 19-20, and 39-40 under 35 U.S.C. § 102(b) be withdrawn.

B. The Rejection Over Faris

The Office Action, at page 6, rejects Claims 1-2, 8-9, 11-12, 16-21, 23-26, and 38-40 as allegedly being anticipated by U.S. Patent No. 6,129,911 to Faris (hereinafter, "Faris"), under 35 U.S.C. § 102(e) for the reasons of record. In sum, the Office Action alleges that Faris discloses methods of isolating progenitor cells from deceased donors or cadavers, neither of which have beating hearts. Applicants traverse respectfully.

Applicants submit respectfully that Claims 1-2, 8-9, 11-12, 16-21, 23-26, and 38-40, as amended, are not anticipated by Faris because Faris does not disclose each and every element of those amended claims as is required for a *prima facie* showing of

anticipation. As noted above for Reid, Faris does not teach or suggest obtaining progenitor cells from donor tissues that are considered unsuitable for transplantation. While Faris does disclose at column 5, lines 6-7, that tissue may be obtained from a deceased donor or an aborted fetus, the method for isolating progenitors actually disclosed by Faris, at column 6, lines 5-23, provides that the isolation process begins immediately following *anesthetization* of the donor, *i.e.*, while the donor is still alive with a beating heart. Accordingly, in view of the teachings of Faris, and in light of the art available at the time which taught that an organ may remain suitable for transplant for a limited time following cessation of the donor's heartbeat, Applicants submit respectfully that one skilled in the art would **not** be taught by Faris that viable progenitor cells could be obtained from organ tissues that had passed the point of irreparable damage so as to be unsuitable for tranplantation, as claimed in the present application.

Accordingly, Applicants submit respectfully that the claims of the present invention, as amended, are not anticipated by Faris, and Applicants request respectfully that the rejection of Claims 1-2, 8-9, 11-12, 16-21, 23-26, and 38-40 under 35 U.S.C. § 102(e) be withdrawn.

II. The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn

The Office Action, at pages 6-9, rejects Claims 21, 23-28, 33-36, and 38-40 as allegedly being obvious, for the reasons of record, over Reid in view of Faris under 35 U.S.C. § 103(a). in sum, the Office Action alleges that Reid teaches methods for isolating liver stem cells from any species. While the Office Action acknowledges

that Reid does not teach specifically that the donor has a non-beating heart at the time when the tissue is harvested or that the tissue is harvested within the claimed time windows, the Office Action alleges that Faris cures these deficiencies by teaching the isolation of adult human liver tissue from adult cadavers. Applicants traverse respectfully.

Applicant submits respectfully that the novel methods of the present invention are neither taught nor suggested by Reid, either alone or in view of Faris. There is neither teaching nor suggestion in these references that, as discussed above, viable progenitor cells may be obtained from organ tissue that is unsuitable for transplantation. The Office Action does not allege that Faris cures this deficiency in Reid. Thus, without acquiescing in the allegation that Faris may be combined with Reid to provide hepatic progenitor cells isolated from adult human cadavers, Applicants submit respectfully that, as Faris fails to cure the deficiencies of Reid with respect to the use of organ tissue unsuitable for transplantation, the combination of the Reid with Faris fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Accordingly, Applicants submit respectfully that the rejection of Claims 21, 23-28, 33-36, and 38-40 under 35 U.S.C. § 103(a) has been traversed, and Applicants request respectfully that the rejection of Claims 21, 23-28, 33-36, and 38-40 under 35 U.S.C. § 103(a) be withdrawn.

III. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

At pages 3-4 of the Office Action, Claims 1, 6-7, 11, 13-15, 23-36, and 39-40 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out particularly and claim distinctly the subject matter regarded as the invention for the reasons of record. In sum, the Office Action alleges that the expression "non-fetal donor tissue that would be considered unsuitable for organ transplantation" and the use of the term "substantially" are unclear, and that Claim 13 is dependent upon itself. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Claims 12, 23, 27, 28, 30, and 39 are amended to delete the term "substantially." Further, Applicants amend Claim 13 to recite the "method of Claim 12."

With regard to the allegation that the expression "non-fetal donor tissue that would be considered unsuitable for organ transplantation" is unclear and not adequately defined in the specification, Applicants respectfully direct Examiner's attention to the following passages from the specification, as filed, which describe and define means of determining the unsuitability of cadaveric liver for organ transplantation: generally, page 21, lines 30-32, recite "Isolation of liver progenitors from cadaver human liver, as disclosed herein, is novel and unexpected due to the prevailing opinion in the art that liver loses its utility due to ischemia." More specifically, page 1, lines 19-20, recite "recent efforts to use such donors have supported the possibility of using them if the liver is obtained within a half hour of death"; page 3, lines 4-6, recite "no organs are

used after heart arrest and, experimentally, none are used after more than one-half hour from the time of heart arrest or asystole"; page 3, lines 15-18, recite "The liver can functionally survive functionally for no longer than one hour and transplants from non-heart-beating donors (NHBDs) are recommended to be carried out preferably within the first thirty-five minutes of exposure to warm ischemia." Accordingly, Applicants submit respectfully that the point at which cadaveric liver would be considered unsuitable for organ transplantation is clear to one skilled in the art.

On this basis, Applicants suggest respectfully that the rejections have been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejections of Claims 1, 6-7, 11, 13-15, 23-36, and 39-40 be withdrawn.

CONCLUSION

Applicants submit respectfully that the present application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

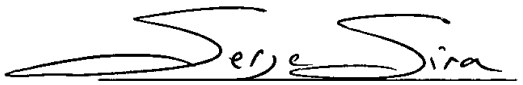
Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should be directed to our address given below.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in

connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,



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